Serial No.: 10/571,510

Filed: December 8, 2006

Page : 2 of 15

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

- 1. (Currently Amended) A composition comprising a beneficial therapeutically active compound covalently bonded conjugated to an adduct of a dialkoxy substance and a guanidinylating reagent.
- 2. (Original) The composition of claim 1, wherein the dialkoxy substance is an acetal or a ketal.
- 3. (Original) The composition of claim 1, wherein the guanidinylating reagent comprises a guanidine or alkylguanidine moiety.
- 4. (Original) The composition of claim 1, wherein the dialkoxy substance comprises at least one cyclic acetal having the formula:

wherein R_1 , R_2 , and/or R_3 groups comprise two or more 5- or 6-membered rings which are linked together by at least one acetal functional group and wherein R_1 - R_2 , and R_3 are the carbon atoms of two separate ring systems.

5. (Previously presented) The composition of claim 4, wherein the cyclic acetal is a glycoside.

Serial No.: 10/571,510

Filed: December 8, 2006

Page : 3 of 15

6. (Original) The composition of claim 5, wherein the glycoside is an aminoglycoside.

- 7. (Cancelled).
- 8. (Previously presented) The composition of claim 1, wherein the dialkoxy substance is selected from the group consisting of amikacin, gentamicin, kanamycin, neomycin, netilmicin, O-2,6-diamino-2,6-dideoxy-beta-L-idopyranosyl-(1 to 3)-O-beta-D-ribofuranosyl-(1 to 5)-O-[2-amino-2-deoxy-alpha-D-glucopyranosyl-(1 to 4)]-2-deoxystreptamine, streptomycin, tobramycin, ouabain, deslanoside, digoxin, digitoxin, lantoside and strophanthin.
- 9. (Currently Amended) The composition of claim 1, wherein the beneficial therapeutically active compound is selected from the group consisting of a nucleic acid, nucleoside, protein, peptide, amino acid residue, lipid, carbohydrate, synthetic organic compound, metal, vitamin, small molecule, dye, isotope, antibody, toxin and ligand.
- 10. (Currently Amended) The composition of claim 1, wherein the beneficial therapeutically active compound comprises a nucleoside, wherein the nucleoside is a reverse transcriptase inhibitor.
- 11. (Original) The composition of claim 10, wherein the reverse transcriptase inhibitor is selected from the group consisting of 3'-azido-3'-deoxythymidine, 2',3'-dideoxyinosine and 2',3'-dideoxycytidine.
- 12. (Original) The composition of claim 10, wherein the reverse transcriptase inhibitor is conjugated to an aminoglycoside.
- 13. (Original) The composition of claim 12, wherein the aminoglycoside is selected from the group consisting of amikacin, gentamicin, kanamycin, neomycin, netilmicin, O-2,6-diamino-

Attorney's Docket No.: 15670-0198US1 / SD2002-135

Applicant: Yitzhak Tor et al. Serial No.: 10/571,510

Filed: December 8, 2006

Page : 4 of 15

2,6-dideoxy-beta-L-idopyranosyl-(1 to 3)-O-beta-D-ribofuranosyl-(1 to 5)-O-[2-amino-2-deoxy-alpha-D-glucopyranosyl-(1 to 4)]-2-deoxystreptamine, streptomycin and tobramycin.

- 14. (Currently Amended) A method of increasing the cellular uptake of a beneficial therapeutically active compound, comprising:
 - (a) modifying a dialkoxy substance by treating the dialkoxy substance with a guanidinylating reagent to form an adduct;
 - (b) conjugating covalently bonding the adduct with to the beneficial therapeutically active compound to form a conjugate; and
 - (c) delivering the conjugate to a cell.
- 15. (Original) The method of claim 14, wherein the dialkoxy substance is an acetal or a ketal.
- 16. (Original) The method of claim 14, wherein the guanidinylating reagent comprises a guanidine or alkylguanidine moiety.
- 17. (Original) The method of claim 14, wherein the dialkoxy substance comprises at least one cyclic acetal having the formula:

$$R_1 R_2$$
 $Q R_3$

wherein R_1 , R_2 , and/or R_3 groups comprise two or more 5- or 6-membered rings which are linked together by at least one acetal functional group and wherein R_1 - R_2 , and R_3 are the carbon atoms of two separate ring systems.

- 18. (Previously presented) The method of claim 17, wherein the cyclic acetal is a glycoside.
- 19. (Original) The method of claim 18, wherein the glycoside is an aminoglycoside.

Attorney's Docket No.: 15670-0198US1 / SD2002-135

Applicant: Yitzhak Tor et al. Serial No.: 10/571,510 Filed: December 8, 2006

Page : 5 of 15

20. (Previously presented) The method of claim 18, wherein in treating the glycoside, the guanidinylating reagent is reacted with at least one primary or secondary alcohol of the glycoside to produce a guanidinoglycoside.

21. (Original) The method of claim 20, wherein the guanidinylating reagent has the general formula:

$$P_1$$
 P_1
 P_2
 P_3

wherein each of P_1 , P_2 and P_3 is, independently, the same or different protecting group, each protecting group having the general structure:

wherein R₂ is a substituted or unsubstituted alkyl, aryl, or heterocyclic group.

- 22. (Previously presented) The method of claim 18, wherein in treating the glycoside, the guanidinylating reagent is reacted with at least one primary or secondary amine of the glycoside to produce a guanidinoglycoside.
- 23. (Previously presented) The method of claim 22, wherein the guanidinylating reagent has the general formula:

Attorney's Docket No.: 15670-0198US1 / SD2002-135

Applicant: Yitzhak Tor et al. Serial No.: 10/571,510

Filed: December 8, 2006

Page : 6 of 15

wherein R_1 is trifluoromethyl group, and each of P_1 , P_2 and P_3 is, independently, the same or different protecting group, each protecting group having the general structure:

$$\mathbb{R}_{2}$$
 \mathbb{C}
 \mathbb{C}

wherein R₂ is a substituted or unsubstituted alkyl, aryl, or heterocyclic group.

24. (Cancelled).

- 25. (Previously presented) The method of claim 14, wherein the dialkoxy substance is selected from the group consisting of amikacin, gentamicin, kanamycin, neomycin, netilmicin, O-2,6-diamino-2,6-dideoxy-beta-L-idopyranosyl-(1 to 3)-O-beta-D-ribofuranosyl-(1 to 5)-O-[2-amino-2-deoxy-alpha-D-glucopyranosyl-(1 to 4)]-2-deoxystreptamine, streptomycin, tobramycin, ouabain, deslanoside, digoxin, digitoxin, lantoside and strophanthin.
- 26. (Currently Amended) The method of claim 14, wherein the beneficial therapeutically active compound is selected from the group consisting of a nucleic acid, nucleoside, protein, peptide, amino acid residue, lipid, carbohydrate, synthetic organic compound, metal, vitamin, small molecule, dye, isotope, antibody, toxin and ligand.

Serial No.: 10/571,510

Filed: December 8, 2006

Page : 7 of 15

27. (Currently Amended) The method of claim 14, wherein the beneficial therapeutically active compound comprises a nucleoside, wherein the nucleoside is a reverse transcriptase inhibitor.

- 28. (Original) The method of claim 27, wherein the reverse transcriptase inhibitor is selected from the group consisting of 3'-azido-3'-deoxythymidine, 2',3'-dideoxyinosine and 2',3'-dideoxycytidine.
- 29. (Original) The method of claim 27, wherein the reverse transcriptase inhibitor is conjugated to an aminoglycoside.
- 30. (Original) The method of claim 29, wherein the aminoglycoside is selected from the group consisting of amikacin, gentamicin, kanamycin, neomycin, netilmicin, O-2,6-diamino-2,6-dideoxy-beta-L-idopyranosyl-(1 to 3)-O-beta-D-ribofuranosyl-(1 to 5)-O-[2-amino-2-deoxy-alpha-D-glucopyranosyl-(1 to 4)]-2-deoxystreptamine, streptomycin and tobramycin.
- 31. (Previously presented) The method of claim 19, wherein in treating the glycoside, the guanidinylating reagent is reacted with at least one primary or secondary alcohol of the glycoside to produce a guanidinoglycoside.
- 32. (Previously presented) The method of claim 19, wherein in treating the glycoside, the guanidinylating reagent is reacted with at least one primary or secondary amine of the glycoside to produce a guanidinoglycoside.
- 33. (Currently Amended) The composition of <u>claim 1elaim 7</u>, wherein the <u>beneficial</u> <u>therapeutically active</u> compound in the conjugate is covalently bonded to the adduct through a linker.
- 34. (Previously presented) The composition of claim 33, wherein the linker is a releasable linker.

Serial No.: 10/571,510

Filed: December 8, 2006

Page : 8 of 15

35. (Previously presented) The composition of claim 33, wherein the linker is a thiol linker or an amine linker.

- 36. (Previously presented) The composition of claim 35, wherein the amine linker is an amino acid linker.
- 37. (Currently Amended) The method of <u>claim 14</u><u>claim 24</u>, wherein the <u>beneficial</u> <u>therapeutically active</u> compound in the conjugate is covalently bonded to the adduct through a linker.
- 38. (Previously presented) The method of claim 37, wherein the linker is a releasable linker.
- 39. (Currently Amended) The composition method of claim 38, wherein the linker is a thiol linker or an amine linker.
- 40. (Previously presented) The composition method of claim 39, wherein the amine linker is an amino acid linker.
- 41. (New) The composition of claim 1, wherein the adduct is a guanidinoaminoglycoside.
- 42. (New) The method of claim 14, wherein the adduct is a guanidinoaminoglycoside.
- 43. (New) The composition of claim 35, wherein the thiol linker is a dithiol.
- 44. (New) The composition of claim 43, wherein the dithiol is β -mercaptoethylether.
- 45. (New) The composition of claim 33, wherein the linker is a hydrolysable linker.
- 46. (New) The composition of claim 35, wherein the amino acid linker is glycine.

Serial No.: 10/571,510

Filed: December 8, 2006

Page : 9 of 15

47. (New) The method of claim 39, wherein the thiol linker is a dithiol.

- 48. (New) The method of claim 47, wherein the dithiol is β -mercaptoethylether.
- 49. (New) The method of claim 37, wherein the linker is a hydrolysable linker.
- 50. (New) The method of claim 40, wherein the amino acid linker is glycine.